

# Psoriasis Is a Complex and Chronic Disease

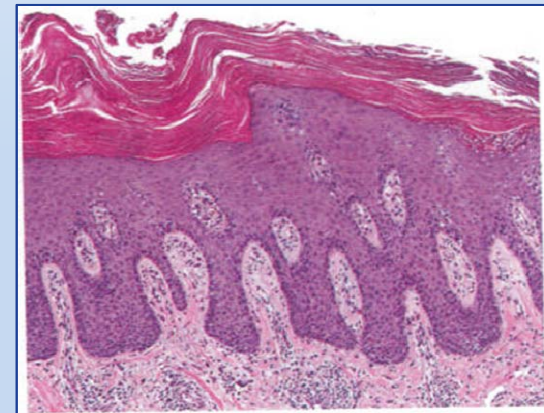
# The Features of Plaque Psoriasis

## ■ Clinical features

- Sharply demarcated, erythematous plaques with silvery-white scale<sup>1,2</sup>
- Common locations include scalp, elbows, and knees<sup>1,2</sup>

## ■ Histologic features

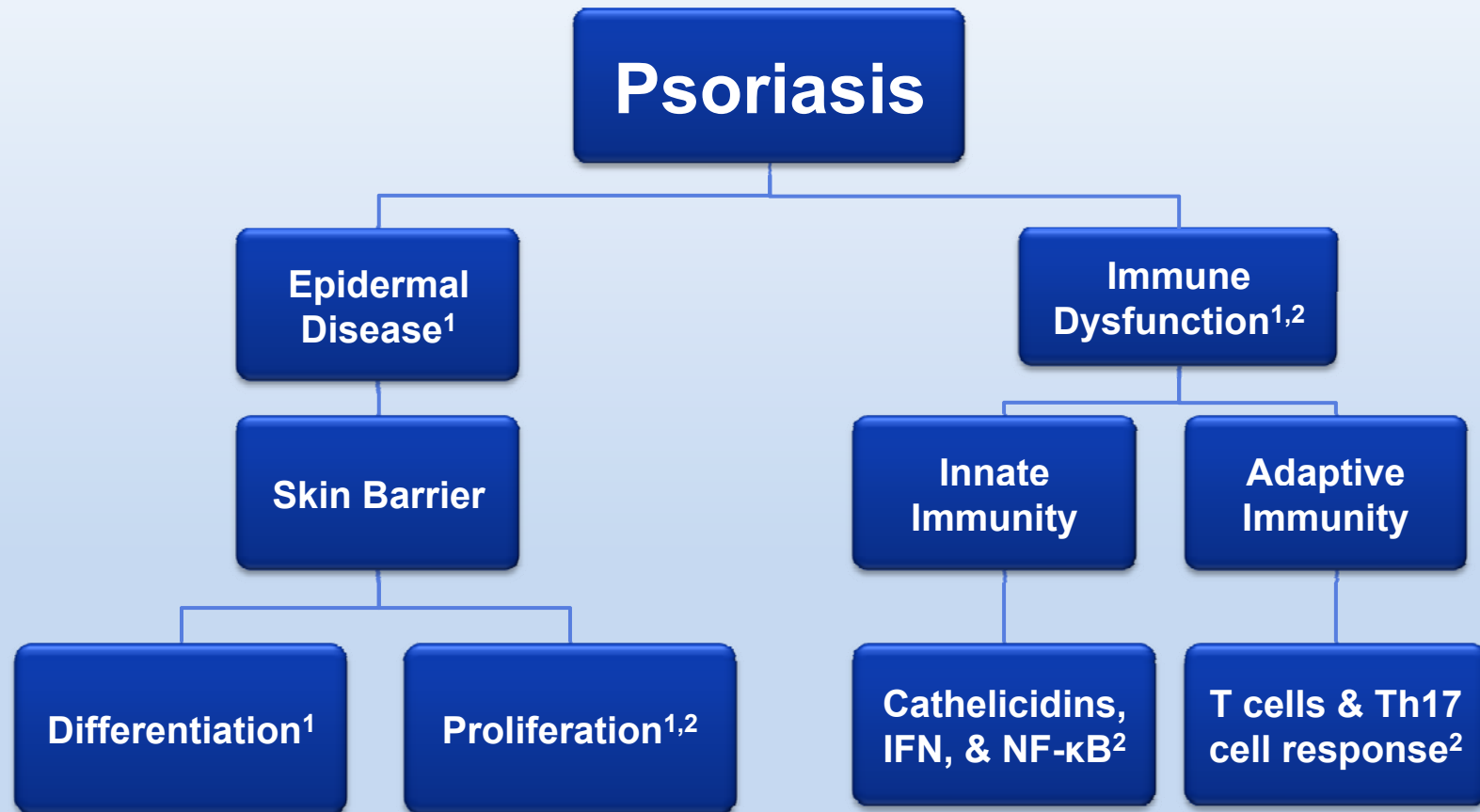
- Hyperproliferation leads to acanthosis (thickened epidermis) and elongated rete ridges<sup>1-3</sup>
- Abnormal keratinocyte differentiation leads to parakeratosis (nucleated cells remaining in the upper layers of the epidermis)<sup>1-3</sup>
- Loss of normal granular layer in the epidermis<sup>2</sup>
- Leukocyte infiltrate forms in the epidermis and dermis<sup>1,2</sup>



# Pathogenesis of Psoriasis

- Once thought to be a disease of the epidermis, now considered to be an immune disorder<sup>1</sup>
- Abnormal activation of leukocytes leads to accumulation of T cells and other immune cells in developing lesions<sup>1</sup>
- Proinflammatory cytokines cause keratinocyte hyperproliferation and altered differentiation; epidermal cell turnover speeds up from normal 28–30 days to 3–5 days<sup>1,2</sup>
- Continued activation of immune cells sustains the psoriatic lesion<sup>3</sup>

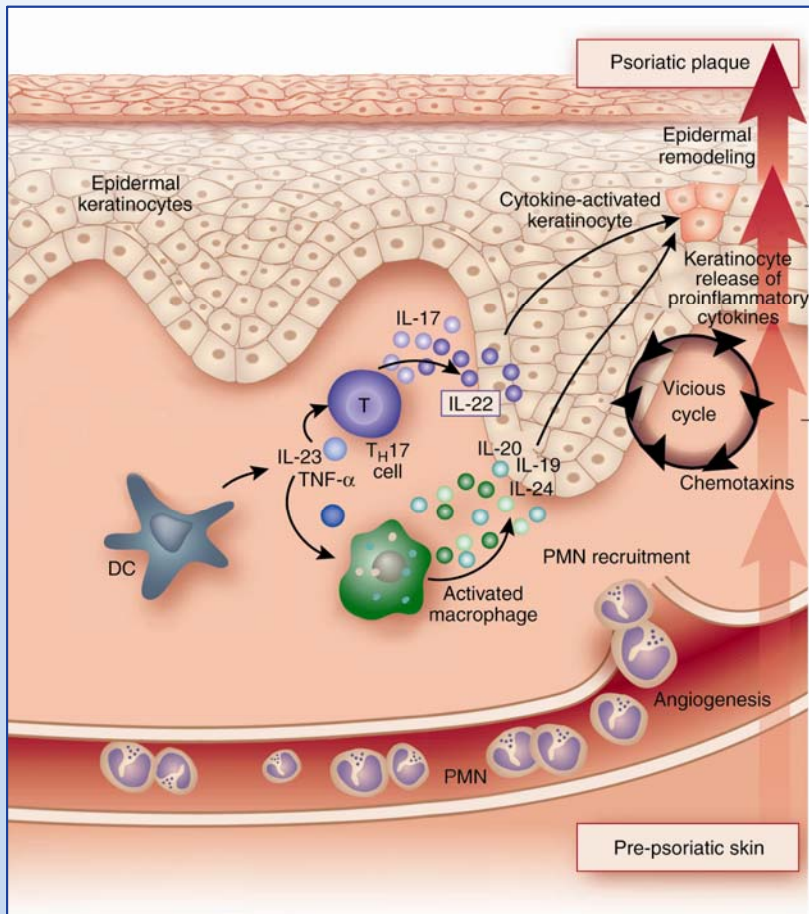
# Psoriasis Is a Complex Disease With Many Different Components



IFN = interferon; NF-κB = nuclear factor kappa-light-chain-enhancer of activated B cells; Th = T helper.

1. Tangheiti EA. *J Drugs Dermatol*. 2009;8(8 Suppl):s4-s8.
2. Nestle FO et al. *N Engl J Med*. 2009;361:496-509.

# Pathogenesis of Psoriasis Is Multifactorial

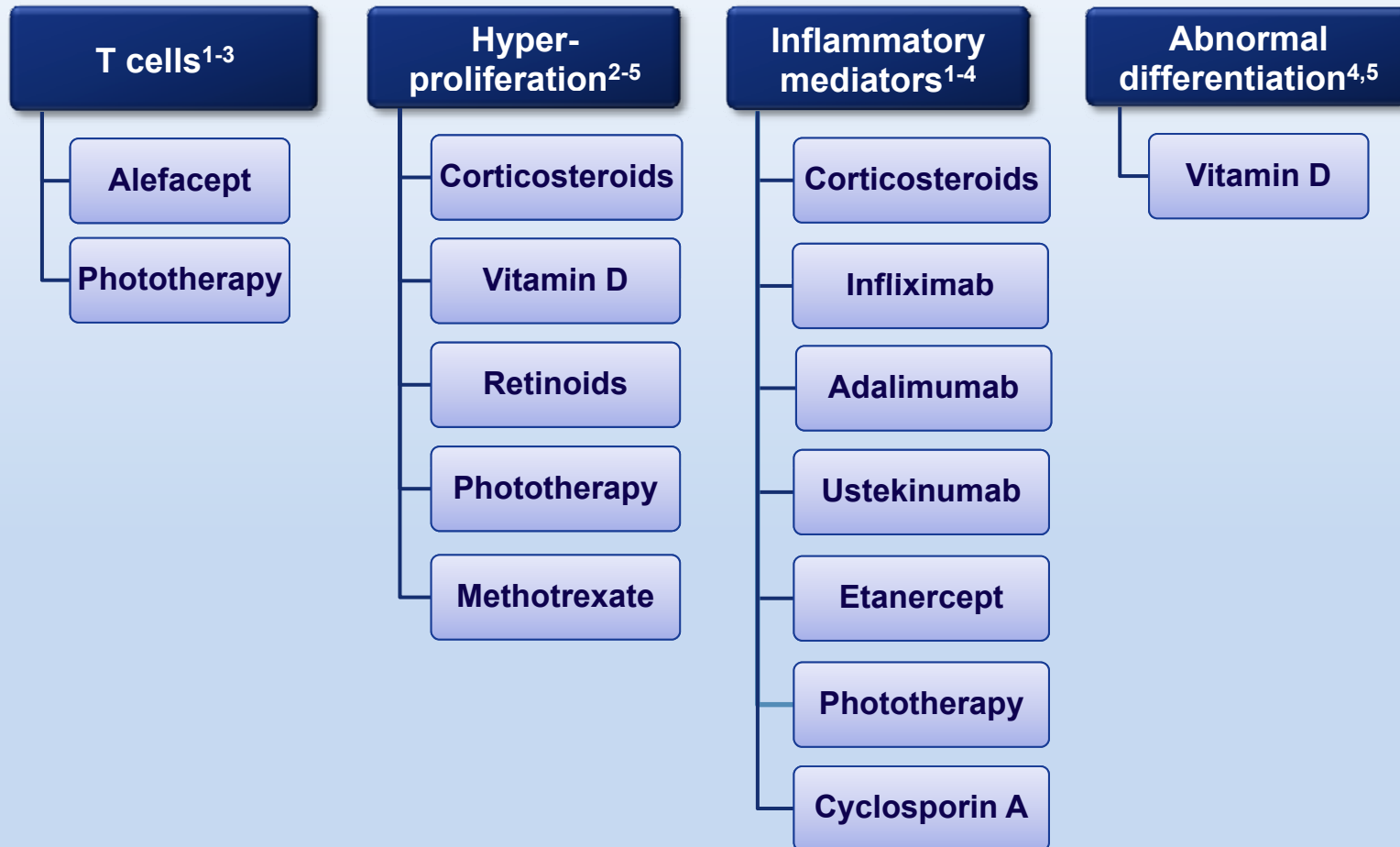


- Both the innate and adaptive immune systems are involved in the pathogenesis of psoriasis, in addition to keratinocyte dysregulation and epidermal dysfunction<sup>1-3</sup>
- No single treatment can address all aspects of this disease

DC = dendritic cell; IL = interleukin; PMN = polymorphonuclear leukocytes; TNF = tumor necrosis factor.

1. Nestle FO et al. *N Engl J Med.* 2009;361:496-509. 2. Tangheiti EA. *J Drugs Dermatol.* 2009;8(8 Suppl):s4-s8. 3. Schön MP, Boehncke WH. *N Engl J Med.* 2005;352:1899-1912. Image source: Nickoloff BJ. *Nat Med.* 2007;13:242-244. Reproduced with permission.

# Treatments for Psoriasis Target Different Aspects of the Disease



1. Nestle FO et al. *N Engl J Med.* 2009;361:496-509. 2. Nickoloff BJ, Nestle FO. *J Clin Invest.* 2004;113:1664-1675. 3. Menter A et al. *J Am Acad Dermatol.* 2010;62:114-135. 4. Menter A et al. *J Am Acad Dermatol.* 2009;60:643-659. 5. Afifi T et al. *Can Fam Physician.* 2005;51:519-525.

# Importance of Topical Treatments for Psoriasis

- Approximately 80% of patients with psoriasis are classified as having mild to moderate disease<sup>1</sup>
- The majority of these patients can be treated with topical medications, which generally are both highly effective and safe<sup>1</sup>
- Topical corticosteroids have been the mainstay of topical psoriasis treatment since the 1950s, but there are a variety of topical treatment options available today<sup>1,2</sup>

## A 4-Week Regimen of Daily Clobex® (clobetasol propionate) Spray, 0.05%, Is an Effective Treatment for Clearing Plaques Quickly



Baseline\*



After 4 weeks of treatment with Clobex® Spray\*

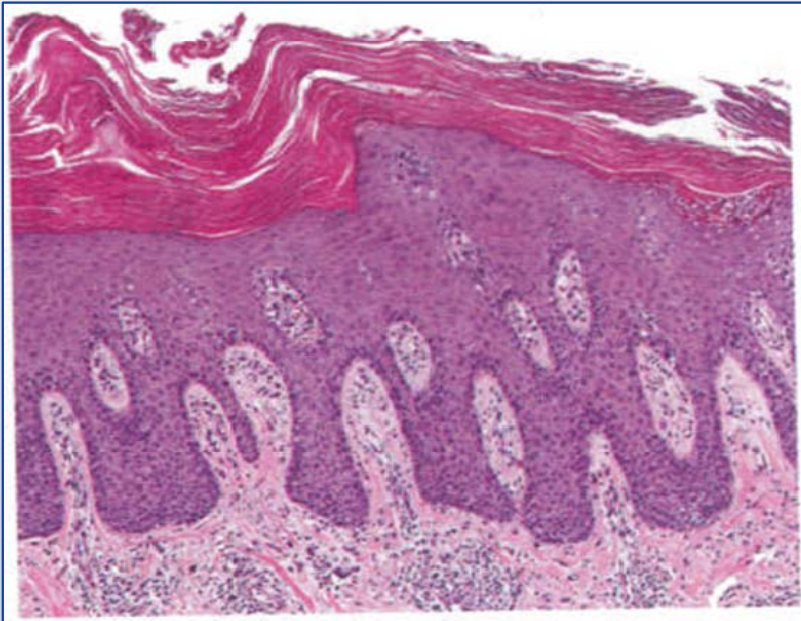
Multicenter, open-label study to evaluate safety and efficacy of a sequential treatment regimen of clobetasol propionate spray, 0.05%, followed by calcitriol ointment, 3 µg/g, in the management of moderate to severe plaque psoriasis.

\*Data on file. Galderma Laboratories, L.P. Fort Worth, TX.

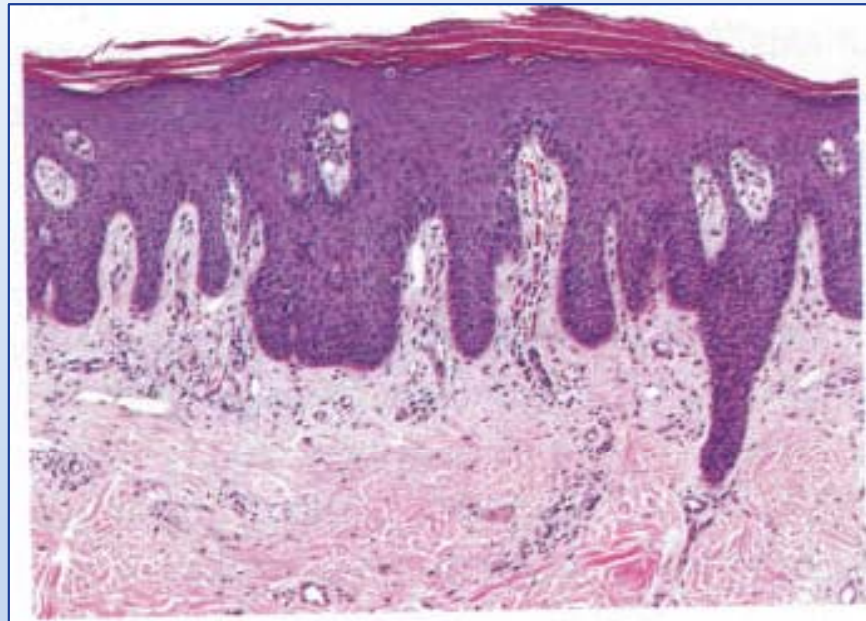
Patient 050-007.

Brodell RT et al. *J Drugs Dermatol.* 2011;10:158-164.

## Lower Layers of Epidermis Remain Dysregulated in Quiescent Lesion Sites



Active edge of psoriatic lesion\*



Inactive psoriatic lesion site\*

\*Untreated lesion.

# Vitamin D<sub>3</sub> and the Skin

- Regulation of cellular differentiation<sup>1</sup>
  - Gene expression in keratinocytes is tightly controlled via interaction between the active metabolite of vitamin D<sub>3</sub> (calcitriol) and its receptor, vitamin D receptor (VDR)
- Restoration of normal epidermal structure<sup>2</sup>
  - Effects of treatment with topical calcitriol
    - Restoration of granular layer
    - Reduced acanthosis and parakeratosis
    - Marked reduction in hyperproliferation and normalization of keratinization
    - Reduction in inflammatory cells penetrating the epidermal layer

# Topical Vitamin D<sub>3</sub> Helps to Restore Normal Keratinocyte Differentiation



- Abnormal cellular differentiation has been shown to contribute to the recurrence of psoriatic plaques<sup>1,2</sup>
- Only topical vitamin D<sub>3</sub> targets abnormal cellular differentiation<sup>2,3</sup>
- Calcitriol has been shown to normalize cell differentiation in psoriatic skin<sup>2-4</sup>
- Vitamin D<sub>3</sub> agents help to delay plaque recurrence<sup>4</sup>

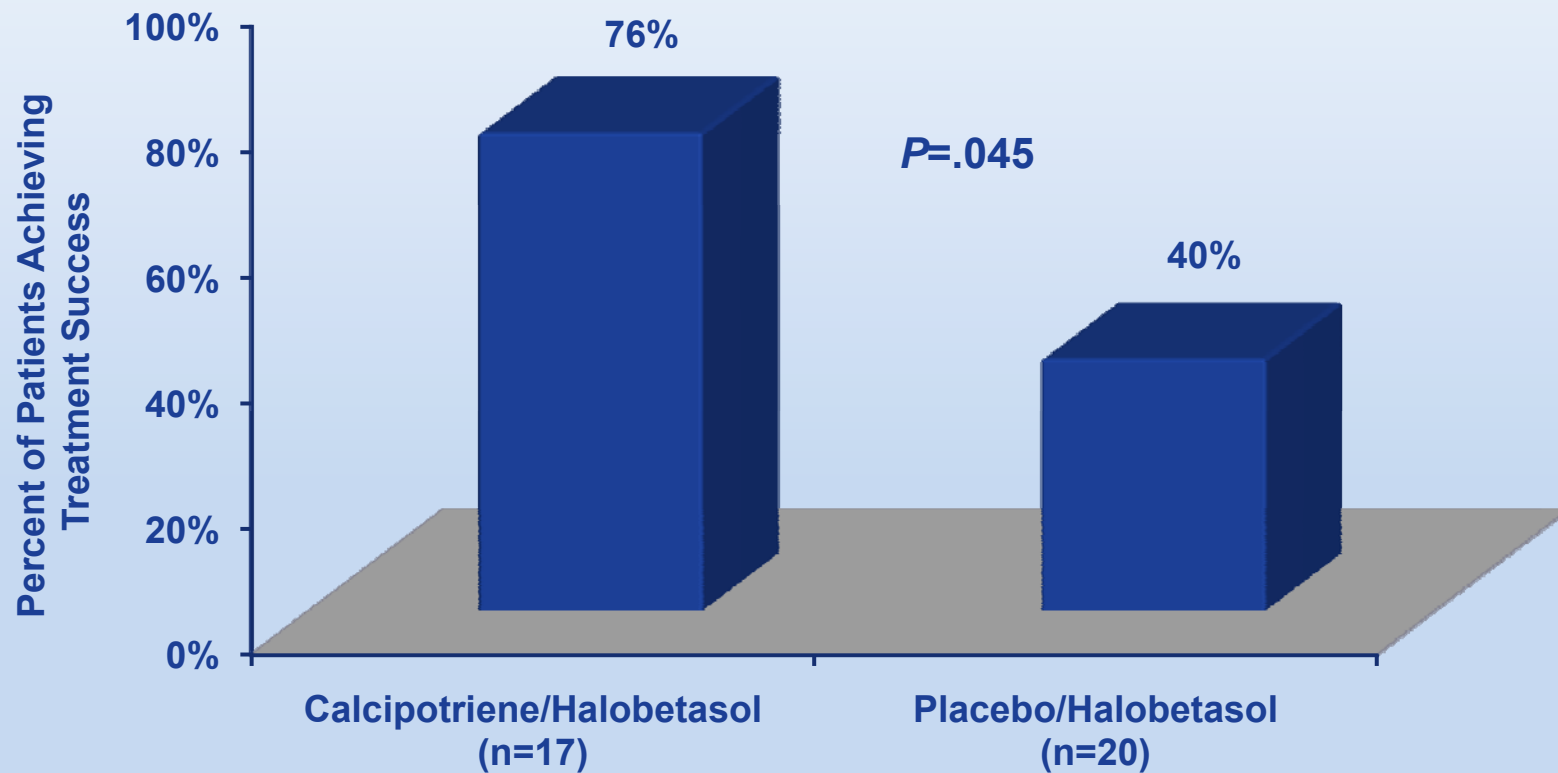
# Topical Vitamin D<sub>3</sub> Helps Prolong Remission

## Long-Term Management With Weekend/Weekday Regimen: Study Design

- 44 patients with mild to moderate psoriasis
- Treatment with calcipotriene in the morning and halobetasol in the evening for 2 weeks
- Patients (n=40) who improved  $\geq 50\%$  after 2 weeks of treatment were randomized to 1 of 2 groups
  - Halobetasol twice daily on weekends and calcipotriene twice daily on weekdays
  - Halobetasol twice daily on weekends and placebo twice daily on weekdays
- Patients evaluated for 6 months with Physician's Global Assessment

# Topical Vitamin D<sub>3</sub> Helps Prolong Remission in Psoriasis Patients

Patients\* Who Achieved Marked Improvement† for 6 Months



\*Patients enrolled in 6-month weekend/weekday regimen had improved at least 50% after 2 weeks of treatment with calcipotriene ointment in the morning and halobetasol in the evening.  
†Remission or treatment success defined as “marked improvement” (≥75% improvement or global evaluation of 2 or less) for 6 months.

Lebwohl M et al. *J Am Acad Dermatol.* 1998;39:447-450.

# Phase III Clinical Data for Vectical® (calcitriol) Ointment 3 µg/g



- In a pivotal trial, 34% of patients with mild to moderate plaque psoriasis treated with Vectical® Ointment achieved treatment success (GSS clear or minimal) at 8 weeks vs 22% with the vehicle (N=418) ( $P=.005$ )<sup>1</sup>
- The most commonly occurring adverse events were lab test abnormality, urine abnormality, psoriasis, hypercalciuria, pruritus, and skin discomfort<sup>2</sup>
- Vectical® has been demonstrated to be safe for up to 52 weeks of use<sup>3</sup>

GSS = Global Severity Score.

1. Lebwohl M et al. *J Drugs Dermatol*. 2007;6:428-435.
2. VECTICAL® (calcitriol) Ointment 3 mcg/g [Prescribing Information]. Fort Worth, TX: Galderma Laboratories, L.P.; 2009.
3. Lebwohl M et al. *Cutis*. 2009;83:205-212.

# Sequential Regimen of 4 Weeks of Clobex<sup>®</sup> Spray Followed by 8 Weeks of Vectical<sup>®</sup> Ointment: Patient Photos



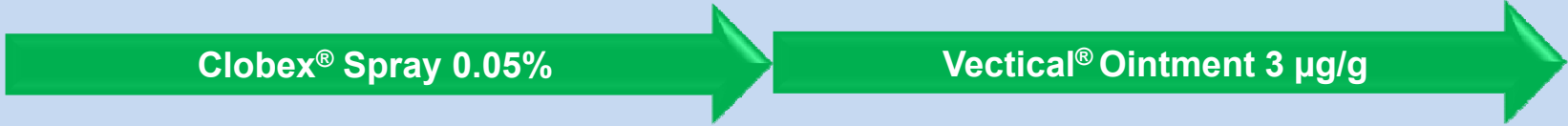
**Baseline**



**Week 4**



**Week 12**



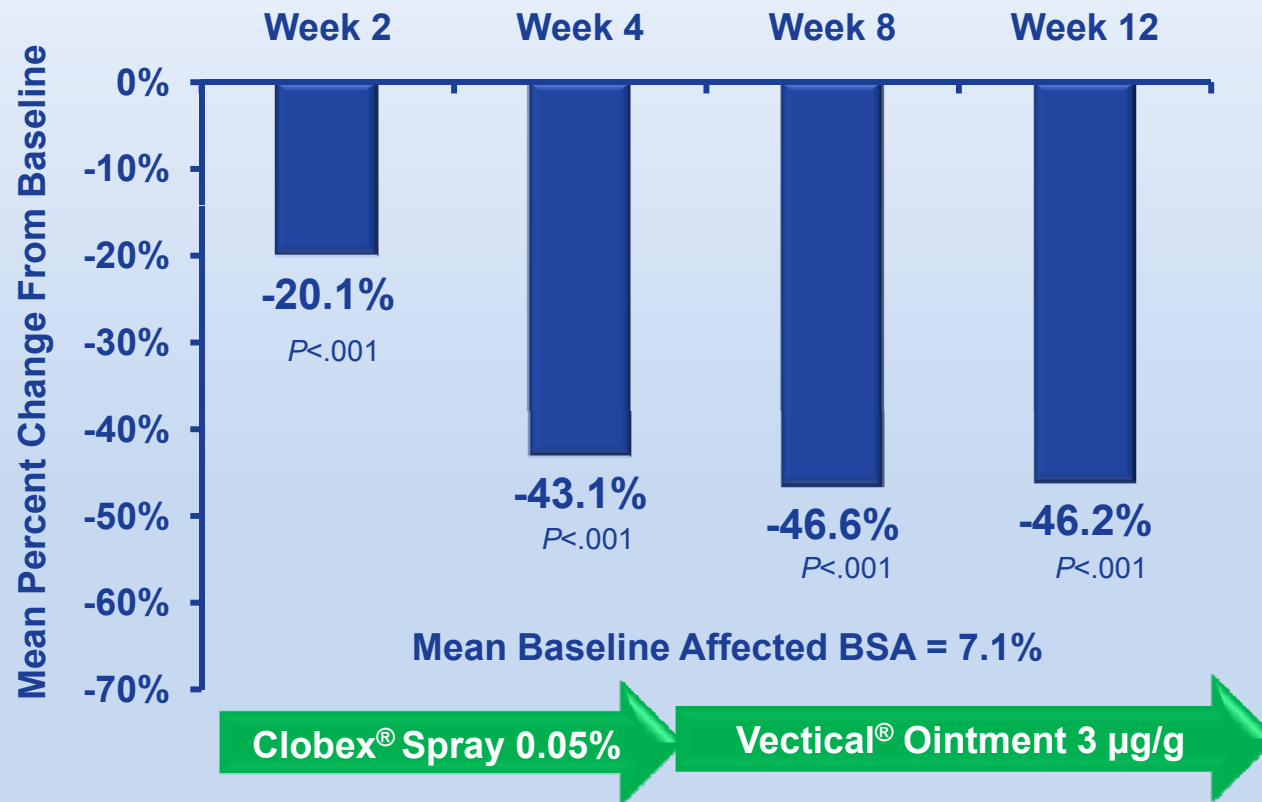
Patient 050-007.  
Consistent with the established safety profile for each drug, adverse events reported were application site irritation, pruritus, stinging/burning, folliculitis, rare skin atrophy, and telangiectasias.

Multicenter, open-label study to evaluate safety and efficacy of a sequential treatment regimen of clobetasol propionate spray, 0.05%, followed by calcitriol ointment, 3 µg/g, in the management of moderate to severe plaque psoriasis (n=170 per protocol).

Data on file. Galderma Laboratories, L.P. Fort Worth, TX.

# Sequential Regimen of 4 Weeks of Clobex® Spray Followed by 8 Weeks of Vectical® Ointment

Affected BSA Remained Stable or Improved for 98.8% of Patients Using Vectical® Ointment<sup>1</sup>



Per-protocol population, n=170<sup>1,2</sup>

P values were computed from a paired t-test and signed rank test for each post-baseline comparison to baseline.

The primary efficacy endpoint was ODS. Treatment success defined as ≥ 1-grade improvement on the ODS scale.  
 Success at week 8 = 100%; Success at week 12 = 84.1%

BSA = body surface area; ODS = Overall Disease Severity.

1. Data on file. Galderma Laboratories, L.P. Fort Worth, TX. 2. Brodell RT et al. *J Drugs Dermatol.* 2011;10:158-164.

# Conclusions

- Psoriasis is a complex and chronic disease<sup>1</sup>
  - Multiple therapies may be needed to address both the acute and chronic aspects of the disease
- Topical corticosteroids play an important role in addressing inflammation and the acute signs and symptoms of psoriasis<sup>2</sup>
- However, abnormal keratinocyte differentiation is a key contributor to plaque formation<sup>3</sup> and will persist if left unaddressed<sup>4,5</sup>
- Topical vitamin D<sub>3</sub> normalizes cellular differentiation and therefore may help to delay plaque recurrence<sup>6</sup>

1. Nestle FO et al. *N Engl J Med.* 2009;361:496-509. 2. Menter A et al. *J Am Acad Dermatol.* 2009;60:643-659. 3. Schön MP, Boehncke WH. *N Engl J Med.* 2005;352:1899-1912. 4. Langner A et al. *J Dermatolog Treat.* 1992;3:177-180. 5. Gerritsen MJP et al. *Br J Dermatol.* 1993;128:666-673. 6. Lebwohl M et al. *J Am Acad Dermatol.* 1998;39:447-450.

# Vectical<sup>®</sup> Ointment: Important Safety Information

Vectical<sup>®</sup> (calcitriol) Ointment 3 mcg/g is a topical treatment for mild to moderate plaque psoriasis in adults 18 years and older.

The most frequent adverse events ( $\geq 3\%$ ) reported in clinical trials were lab test abnormality, urine abnormality, psoriasis, hypercalciuria, pruritus and skin discomfort. Vectical<sup>®</sup> should be used with caution in patients with known or suspected disturbances in calcium homeostasis, who are taking calcium or Vitamin D supplements or who are on diuretics. If aberrations in parameters of calcium metabolism occur, discontinue use until these normalize. Caution patients to avoid excessive exposure to natural or artificial sunlight after applying the ointment. Avoid contact with eyes, lips and face. Limit use to 200 grams per week.

# Clobex® Spray: Important Safety Information

- Approved for treatment of moderate to severe plaque psoriasis affecting up to 20% of body surface area (BSA) in patients 18 years of age or older
- Clobex® (clobetasol propionate) Spray, 0.05%, has been shown to suppress the HPA axis at the lowest doses tested
- Clobex® (clobetasol propionate) Spray, 0.05%, should not be used in the treatment of rosacea or perioral dermatitis and should not be used on the face, groin, or axillae
- In controlled clinical trials, the following adverse reactions have been reported: burning, pruritus, hyperpigmentation, infections and infestations, nasopharyngitis, upper respiratory tract infections, and skin and subcutaneous tissue disorders
- Treatment should be limited to 4 weeks. Treatment beyond 2 weeks should be limited to localized lesions of moderate to severe plaque psoriasis that have not sufficiently improved after the initial 2 weeks of treatment with Clobex® (clobetasol propionate) Spray, 0.05%
- Total dosage of Clobex® (clobetasol propionate) Spray, 0.05%, should not exceed 50 g (59 mL or 2 fl oz) per week
- Clobex® (clobetasol propionate) Spray, 0.05%, is not recommended for use on anyone younger than 18 years of age